Conclusions: Apelin treatment prevents Ang II-mediated hippocampal inflammation and oxidant injury in the hypertensive mice through activation of the BDNF/eNOS/NO signaling pathway, implicating beneficial effects of the Apelin-APJ system on the brain of hypertensive mice. Apelin may represent a potential candidate to treat cardiovascular and cerebrovascular diseases.

GW25-e4432

Enhanced inhibitory effects of amiodarone on hERG channels due to a mutation A561V linked to long QT syndrome type 2

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Objectives: This study was to determine the potential of A561V on the response of hERG channels to amiodarone and the mechanisms underlying the amiodarone-induced long QT syndrome.
Methods: A561V-hERG plasmids were transfected into the HEK293 cells stably expressing WT-hERG channels to mimic heterozygous mutant (WT+A561V-hERG). Whole-cell patch clamp was used to evaluate electrophysiological consequences. Laser confocal scanning microscopy was used to evaluate the membrane distribution of hERG channel protein using a green fluorescent protein tagged to the N-terminus of hERG.
Results: In comparison of WT-hERG channels exposed to amiodarone, heterozygous A561V-hERG channels showed significant decrease in the maximal density of tail currents in the presence of amidarone. The maximal density of tail currents was 52.7±6.65 pA/pF and 29.5±3.29 pA/pF for WT-hERG, 15.79±2.58 pA/pF and 9.27±1.43 pA/pF for heterozygous A561V-hERG, under control condition and exposed to amiodarone, respectively Additionally, A561V-hERG also altered the potential of amiodarone on the gating properties of hERG channels, including activation, steady-state inactivation, recovery from inactivation and deactivation. Images of amiodarone-treated cells expressing heterozygousA561V-hERG showed a severe retention of protein in the endoplasmic reticulum and significant reduction of protein expression on the membrane in HEK293 cells, compared to the counterparts of WT-hERG.
Conclusions: Amiodarone exerts a powerful inhibitory effect on the heterozygous A561V-hERG channels, suggesting the additive suppression of WT-hERG currents by A561V-hERG and amiodarone. This may explain the increased risk of drug-induced LQTS and its propensity to severe arrhythmias in congenital LQT2 individuals receiving amiodarone.

GW25-e5208

Rosiglitazone decreases acute hyperglycemia through restoration of hepatic insulin signaling in rat following myocardial infarction

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Objectives: Stress hyperglycemia is a common pathological feature during the early phase after acute myocardial infarction (AMI). Despite this, it is not clear whether the insulin signaling cascades are perturbed after AMI. It is also unknown whether the impairment of insulin signaling is etiological for hyperglycemia.

In this study, we evaluate 1) the alteration of insulin signaling cascades in major insulin responsive tissues in a rat AMI model, 2) the role of insulin sensitizer rosiglitazone (Ros) in potentiating insulin signaling and reducing hyperglycemia after AMI.
Methods: The left anterior descending coronary artery of male rats was ligated in the MI group. Rosiglitazone (4mg/kg) was administrated in rats 5min before ligation in the MI+Ros group. After 30 minutes of ligation, rats were injected with insulin or PBS intraperitoneally and sacrificed 5 minutes later. Plasma glucose and insulin levels were measured. Expression and/or phosphorylation of insulin receptor β subunit (IRβ), insulin receptor substrate1 (IRS1), IRS2, IRSs-associated p85 subunit of PI3K and Akt in liver, skeletal muscle and heart tissues were determined.
Results: Successful MI was confirmed by increased CK-MB release and enlarged myocardial infract aera by 2, 3, 5-triphenyltetrazolium chloride (TTC) staining. The plasma glucose levels in MI rats was significantly elevated at 5min of ligation ($P<0.01$) and increased gradually with the concentration reached 3.4 times than that of sham controls at 30min. Similarly, rapid increase of insulin concentration in MI groups was observed. Ros administration significantly decreased glucose and insulin levels in AMI rats.

Although the expression of IRβ and IRS1 was comparable in liver tissue in MI and control rats, insulin-stimulated tyrosine phosphorylation of IR and IRS1 were significantly reduced in MI rats. Similarly, the downstream key molecules such as the attachment of PI3K p85 subunit to IRS1 was significantly impaired, together with the phosphorylation of Akt on ser473 in MI rats compared with control rats. By contrast, the expression and phospharylation levels of IRS2, and IRS2-associated p85 in liver were not significantly different among all groups of rats. Ros treatment markedly improved insulin-stimulated phosphorylation of IRβ, IRS1 and Akt in liver tissue of MI rats.

No significant differences were observed for the phosphorylation levels of IRβ, IRS1 and Akt in skeletal muscle or heart among MI and control rats.
Conclusions: Insulin signaling cascades were impaired in liver of rats after AMI. Ros could potentiate insulin signaling in liver tissue and alleviate systemic metabolic disorders, suggesting impairment of insulin signaling promote hyperglycemia in the setting of AMI.

GW25-e1670

The Myocardial Protection Effects of STV-1Na on Rats with Myocardial Infarction

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Objectives: To observe the myocardial protection effects of STV-1Na (a kaurane of natural origin) on Sprague-Dawley (SD) rats with myocardial infarctions (MI).
Methods: SD rats were randomly assigned to Myocardial infarction group (MI) (n=30), sham group (S) (n=30), MI-Trimetazidine group (MT) (0.03mg/100g, n=30), MI-low dose (ML) (0.05mg/100g, n=30), MI-middle dose (MM) (0.1mg/100g, n=30) and MI-high dose (MH) STV-1Na group (0.4mg/100g, n=30). The MI model was set up in SD rats by permanent ligation of the left anterior descending coronary artery (LAD).Sham group suture were through the LAD without ligation. Before and after MI, in MI group and MI-T group normal saline and Trimetazidine were given by gavage, and different dose groups of STV-1Na were given by gavage. The changes of serum cTnI were observed at 8th, 24th, 48th hour after MI. In 1 week, 2 weeks, and 4 weeks after treatment, the area of myocardial infarction were analyzed, maximal rate of left ventricular pressure (dp/dt_{max}) and minimum rate of left ventricular pressure rise (dp/dt_{min}) were measured to evaluate the effects of STV-1Na. The statistical significance of differences was analyzed using SPSS 13.0 for Windows. Groups were compared with one-way analysis of variance (ANOVA) test. A value of $P< 0.05$ was considered statistically significant.
Results: At 8th hour after MI the serum cTnI level of each group was no statistically significant difference ($P>0.05$). But ML, MM, MH and MT group decreased the serum cTnI level significantly at 24th hour after MI ($P<0.01$) (MI (42.3±5.4 ng/ml), ML (17.0±4.3 ng/ml), MM (21.3±3.7 ng/ml), MH (22.2±6.5 ng/ml), MT (22.7±5.3 ng/ml)). ML group and MM group decreased the serum cTnI level ($P<0.05$), and MH group decreased significantly the serum cTnI level ($P<0.01$) at 48th hour after MI (MI (3.7±0.9 ng/ml), ML (1.3±0.7 ng/ml), MM (1.3±0.8 ng/ml), MH (1.0±0.4 ng/ml)). ML group and MM group decreased the myocardial infarction area ($P<0.05$), MH group and MT group decreased the myocardial infarction area significantly ($P<0.01$) (MI (0.362±0.027), ML (0.284±0.027), MM (0.268±0.023), MH (0.254±0.011), MT (0.248±0.021)). In 1 week after MI, MM group, MH group and MT group increased dp/dt_{max} ($P<0.05$). The dp/dt_{max} were no significant difference ($P>0.05$) between ML group and MI group. (MI (6702±329), ML (7276±221), MM (7782±195), MH (7729±172), MT (7535±265)). The dp/dt_{min} in MT group and ML, MM, MH group were no statistically significant difference ($P>0.05$) (MI (-5400±339), ML (-5690±449), MM (-5564±204), MH (-5646±316), MT (-5511±400)). In 2 weeks after MI, MT group (8101±313) and ML, MM, MH group increased the dp/dt_{max} significantly ($P<0.01$). (MI (5868±412), MT (8101±313), ML (7658±392), MM (8499±343), MH (7521±385)) ; MT group, ML group and MM group decreased the dp/dt_{min} ($P<0.05$). The dp/dt_{min} were no difference between MH group and MI group ($P>0.05$) (MI (-4750±463), MT (-6514±493), ML (-6275±623), MM (-7305±491), MH (-5676±640)). In 4 weeks after MI, MT group, ML group, MM group and MH group increased the dp/dt_{max} significantly. (MI (5876±200), MT (7629±374, $P<0.01$), ML (7264±348, $P<0.05$), MM (7743±242, $P<0.01$), MH (7537±185, $P<0.01$)).MT group, MM group and MH group decreased the dp/dt_{min} significantly ($P<0.05$); ML group didn't no decreased the dp/dt_{min} significantly ($P>0.05$) (MI (-4546±279), ML (-5528±505), MT (-5883±436), MM (-6132±533), MH (-5801±343)).
Conclusions: STV-1Na has myocardial protection effects on myocardial infarction and improves myocardial systolic and diastolic function in SD rats with acute myocardial infarction. The effects of STV-1Na were as good as the effects of Trimetazidine.

GW25-e3375

Effect of Myocardial Ischemic Postconditioning Protects Reperfusion Injury in Diabetic and Pharmacological Postconditioning

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Objectives: Clinical studies in patients with acute myocardial infarction have demonstrated that Postconditioning (IPO) was effective in reducing infarct size. We studied cardioprotection of IPO in diabetic heart existence or no, and how to wake-up and recovery cardioprotection of IPO in diabetic heart, whether the diabetic heart is amenable to ischaemic postconditioning is an important unanswered question. Previous studies have demonstrated that postconditioning signals through the PI3K-Akt kinase pathway. Other studies have documented impaired PI3K-Akt signalling in the diabetic myocardium. We hypothesised that due to impaired signaling through the PI3K-Akt pathway, postconditioning does not protect the diabetic heart.
Methods: Diabetic cardiomyopathy rats was induced by intraperitoneal streptozotocin (STZ, 30mg/kg) injection.One week following STZ injection, and blood glucose levels>120 mg/dL were included in the study. high-fat diet rats receiving high-saturated-fat diet consisting of 35% fat, 35% carbohydrates, and 22% protein for 4 weeks.Hearts were rapidly excised and immediately mounted on Langendorff-perfusion apparatus. Perfusion was maintained at a constant pressure of 75 mmHg.Isolated hearts were obtained from two groups: healthy controls (n=10), streptozotocin (STZ) +HFD-induced diabetes (n=12). All hearts underwent 25 min ischemia and